SUMMARY OF SAFETY AND PROBABLE BENEFIT

1. General Information

Device Generic Name:	Ventricular Assist Device (VAD)
Device Trade Name:	DeBakey VAD® *Child* System for Humanitarian Use in Pediatric Patients
Applicant's Name and Address:	MicroMed Technology, Inc 8965 Interchange Drive Houston, TX 77054
Humanitarian Device Exemption (HDE) Number:	H030003
Date of Humanitarian Use Device Designation:	June 10, 2003
Date of Panel Recommendation:	Not applicable (see section 12)
Date of Good Manufacturing Practices Inspection:	July 19, 2002, June 4 and 12 and September 23, 2003
Date of Notice to Applicant:	FEB 25 2004

2. Indications for Use

The DeBakey VAD® *Child* is indicated for use to provide temporary left side mechanical circulatory support as a bridge to cardiac transplantation for pediatric patients (5 – 16 years old, with BSA ≥0.7 m^2 and <1.5 m^2) who are in NYHA Class IV end-stage heart failure, are refractory to medical therapy and who are (listed) candidates for cardiac transplantation.

3. Contraindications

The DeBakey VAD® *Child* is contraindicated in:

- Patients under 5 years of age or with body surface area < 0.7 m^2
- Patients suffering from right ventricular failure unresolved by medical therapy
- Patients with a primary coagulopathy or platelet disorders
- Patients with an allergy or sensitivity to Heparin

4. Warnings and Precautions

See Warnings and Precautions in the final labeling (Directions for Use)

5. Device Description

The DeBakey VAD® *Child* is a miniaturized continuous axial flow valveless blood pump, or ventricular assist device (VAD) that operates with the left ventricle. Capable of producing blood flows between 1 and 10 liters per minute with speeds varying from 7,500 to 12,500 RPM, the DeBakey VAD® *Child* consists of four major subsystems and assorted accessories. The four subsystems include the following:

- DeBakey VAD® *Child* Implantable Pump System
- External Controller
- Clinical Data Acquisition System (CDAS)
- Patient Home Support System (PHSS)

Accessories include:

- VADPAK
- SmartPAK Batteries
- ChargePAK Battery Charger
- Shower Kit

5.1. DeBakey VAD® Child Implantable Pump System

The pump system includes the titanium pump with attached titanium inlet/inflow cannula, outflow graft, percutaneous cable, and implantable flow probe. Within the pump housing is a hermetically sealed blood tube containing the flow-straightener, inducer/impeller and diffuser. The flow-straightener minimizes turbulence created as blood enters the tube from the left ventricle. The rotating action of the inducer maintains uni-directional flow and propels blood forward towards the diffuser; the directional guidance from the diffuser, along with the rotating action of the inducer, forces blood into the outflow graft. The ultrasonic flow probe is placed over the distal end of the outflow graft and provides direct measurement of blood flowing through the outflow graft from the blood pump.

5.2. External System Controller

The Controller is a completely external microprocessor-based unit that contains the circuitry necessary to operate the implanted DeBakey VAD® *Child*. The Controller is connected to the VAD through the percutaneous cable, and displays pump operating parameters and battery life, operates the VAD System alarms and alerts, and contains a sophisticated restart algorithm that attempts to restart the pump in case of desynchronization.[1] The Controller is the primary interface between the VAD and the power source. Two external 12-volt DC nickel metal-hydride (NiMH) batteries power the Controller; battery operation allows the patients to ambulate freely. Two Controllers are supplied at each implant: a primary unit and a back-up unit. Additional power sources for the Controller are the CDAS and PHSS.

5.3. CDAS

The CDAS is for inpatient use only and is the primary power source during implant and immediately post-operatively in the ICU. Consisting of a computer and a data/power isolation unit, the CDAS is used by the physician to establish and adjust system operating parameters and alarm thresholds, and to monitor the pump flow waveform. Communicating with the Controller, the CDAS can acquire and store real-time performance data for the DeBakey VAD® *Child*, as well as historical performance (Holter) data when operational information is downloaded for review. Using the CDAS, the physician can make adjustments to operating parameters, indicated by the historical data and the patient's clinical status.

5.4. PHSS

The PHSS serves three functions, which it can perform simultaneously. The PHSS provides power to the Controller during periods of extended sedentary (tethered) operation using standard wall current (mains), is capable of charging up to 4 rechargeable batteries at a time, and functions as an uninterrupted power supply in the case of mains disconnect or mains power failure. The PHSS can be used by the patient both in and outside the hospital setting.

[1] Desynchronization is the momentary loss of back EMF (electromotive force) commutation where the Controller stops and restarts the pump in approximately 2 seconds.

5.5. *Accessories*

5.5.1. VADPAK

The VADPAK is a pouch consisting of a battery interface board and interface ports that connect the Controller to the batteries; the VADPAK holds both the Controller an the batteries (2) and serves as an external interface when a valid power supply (PHSS or CDAS) is connected to the Controller via the interface ports.

5.5.2. SmartPAK Batteries

The batteries that power the DeBakey VAD® *Child* are nickel metal hydride (NiMH), type DR 36 "smart" batteries. Each battery contains an integrated charge indicator that when activated represents the maximum charge the battery may contain in 25% increments. Each battery will power the VAD for approximately 2.5 – 4 hours, for a combined total battery time of approximately 5 – 8 hours.

5.5.3. ChargePak

The ChargePak is a portable battery charger. It can be used in place of the PHSS for battery charging *only*.

5.5.4. Shower Kit

The Shower Kit is comprised of a Shower Bag and literature containing instructions for proper use. The Shower Bag, when properly used, offers the patient an opportunity to maintain good hygiene by protecting all external components of the DeBakey VAD® System from water damage and eliminating the risk of water contacting any external surfaces of the Controller and batteries during bathing.

5.6. *Safety Elements*

A number of safety elements are incorporated into the DeBakey VAD® *Child* including:

- 24 hour technical support
- Complete backup system on hand at each hospital
- Back up Controller and batteries, and battery pocket for each patient
- Internal battery for Controller alarm for both batteries disconnected
- Audible and visual alarms including low flow, excess current and battery discharged
- Automatic restart algorithm
- Fail-Safe mode for Controller
- Keyed configuration connectors
- Directions For Use

Note: All System components are dedicated to one patient and are intended for repeated use by the original patient, with the exception of the Clinical Data Acquisition System and the Patient Home Support System. Both the CDAS and the PHSS can be used for multiple patients but only on one patient at a time. The CDAS is designed for use only by the clinician in a hospital setting. The PHSS is for use by the patient in both the inpatient and outpatient setting.

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6. Alternative Practices and Procedures

The methods currently available to treat left ventricular failure in children age 5 years to 16 years are limited, and include medical management, mechanical circulatory support and surgical intervention.

- Pharmacological agents to enhance cardiovascular function
- Commercially available extracorporeal ventricular bypass (assist) devices (Thoratec), centrifugal pumps and extracorporeal membrane oxygenation (ECMO)
- Cardiac transplantation, but only when an appropriate donor heart becomes available, is limited by the number and size of available donor hearts and by those transplant candidates on the UNOS waiting list.

7. Marketing History

There is no marketing history for the DeBakey VAD® *Child*. The DeBakey VAD® *Child* is a modification of the DeBakey VAD® System. The DeBakey VAD® System received the CE mark for marketing in Europe in April 2001. In 2002, the CE Mark was awarded for the CBAS™ (Carmeda™ Bioactive Surface) addition. As of 04/15/2003, approximately 156 DeBakey VADs have been sold in Turkey and in the European Community in Germany, Italy, France, Switzerland, and Austria. The DeBakey VAD® has not been withdrawn from any country for any reasons related to the safety or efficacy of the device.

8. Adverse Events

8.1. Potential Adverse Events

Based on a review of published literature on other ventricular assist devices, the risks usually associated with those devices and the data obtained from the DeBakey VAD® worldwide experience, the potential medical risks associated with use of the DeBakey VAD® *Child* include the following adverse events:

- Bleeding
- Reoperation
- Hemolysis
- Infection (all cause)
- Renal dysfunction
- Respiratory dysfunction
- Hepatic Dysfunction
- Cardiac arrhythmias (atrial or ventricular)
- Myocardial Infarction
- Right ventricular dysfunction
- Neural dysfunction
- Thromboembolism
- Mechanical or electrical failure
- Psychiatric events

Note: Adverse events may also occur from any of the risks usually associated with cardiac surgery

9. Summary of Preclinical Studies

9.1. Bench Testing

9.1.1. In Vitro Testing

Extensive laboratory testing was performed on each component of the DeBakey VAD® System to demonstrate that each system component, as well as the integrated system, meets the intended functional requirements as defined in the product specifications and

risk analyses. All requirements of the device design were tested and verified. All system components and the integrated system met all performance requirements and specifications. Major areas of testing included: 1) design and construction features (major components, physical characteristics, pump interface [percutaneous cable], biocompatibility, sterilization and particulates), 2) performance requirements (pump output, service life, flow rate sensor and device measurement methods, ranges and accuracy), and 3) operational requirements (temperature, defibrillation, high power electrical fields, electromagnetic susceptibility, electrostatic discharge, vibration, humidity and ultrasonic energy).

9.1.2. Bio Compatibility Testing

In vitro and *in vivo* biocompatibility studies for the DeBakey VAD® were performed on all materials with direct tissue or fluid contact. The studies were performed in accordance with *International Standards Organization (ISO) 10993 – 1 – 1997 Biological Evaluation of Medical Devices – Parts 3, 4, 5, 6, 10 and 11.* All materials with direct tissue or fluid contact were considered biocompatible.

9.1.3. Reliability Testing

The DeBakey VAD® System was subjected to life testing performed under simulated physiological worst-case conditions for a period of 12 months. The Weibull Model was employed to estimate the sample size necessary to achieve 80% reliability for a 90-day survival with 70% confidence. A sample size of 12 was chosen for the study. No more than 1 of the 12 systems could fail during the period of a successful evaluation. The MicroMed Pulsatile Loop (MPL) provided a thermally controlled pulsatile environment designed to simulate complete support for profound left ventricular failure creating the highest loads on the system since it requires high pump speed (high radial loads). It also created the largest delta pressure across the pump (high thrust loads) and required the highest flow.

Note: The DeBakey VAD® *Child* implantable pump is a modified version of the DeBakey VAD®; the modifications did not require new life testing.

9.2. Laboratory Testing

9.2.1. Animal Studies

A series of *in* vivo animal studies were performed on the DeBakey VAD® to assess system reliability, pump operation, hemodynamic stability, organ function and pathology, and to demonstrate the safety and readiness of the DeBakey VAD® for clinical implantation as a bridge to cardiac transplantation.

Eight devices at two investigative sites were implanted into calves (bovine) weighing between 90-120 kg, and operated continuously for 60 days. One animal was excluded from the study due to surgical error. After 60 days of continuous support, the animals demonstrated no clinical signs indicative of device failures or other device-related abnormalities. The rate of thromboembolism was (14%) in animals and there were no incidences of infection at any site. There were no changes in end organ function as measured by creatinine, basal urea nitrogen or total bilirubin. There were no incidences of mechanical failure. Specific analyses related to device performance indicated that the device performed as intended in the animal recipients.

10. Summary of Clinical Studies

The following information on the adult DeBakey VAD® System worldwide experience is presented in support of use of the DeBakey VAD® *Child* in the proposed pediatric population.

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10.1. Worldwide Overview

As of December 31, 2003, 229 patients have been implanted with the DeBakey VAD® across 26 centers in Europe and the United States. Four trials were conducted worldwide, 2 in Europe and 2 in the U.S. Of the 4 trials, 2 were conducted and completed to evaluate the safety and effectiveness of the DeBakey VAD® as a bridge to transplant; data analysis is ongoing in 1 trial. A third trial evaluated the safety and effectiveness of the Carmeda-coated (Carmeda BioActive Surface: CBAS™) DeBakey VAD®; adverse events are still being adjudicated. The fourth trial, a Phase II pivotal trial in the U.S. is ongoing. Where available, data for the Phase II pivotal trial are included in this submission.

The following tables represent patient distribution and patient disposition worldwide for clinical trials; commercial data where available is also included. As noted in Sub-Section 10.2.4 of this document: Results of the U.S. Feasibility Trial, survival to transplant rates are higher in the U.S. when compared to the European experience (Sub Sections 10.2.4 and 10.3.4): mostly due to the earlier experience in Europe allowing U.S. physicians to take advantage of the learning curve and since patient selection in the U.S. Feasibility Trial was regulated by FDA mandates. As a result, data from the U.S. Feasibility trial best represents the capability of the DeBakey VAD®. Of note, however, is that pump performance and clinical adverse events are similar between the two geographical regions.

Table 1 **Worldwide Patient Distribution**

Centers = 26	***N=229****
Europe	171
Bridge to Transplant Trial	78
CBAS™ Trial	56
Commercial Implantation	37
U.S.	58
Feasibility Trial: bridge to transplant	30
Phase II Pivotal Trial: bridge to transplant	28
Support Duration	
Cumulative Support Duration	53.8 years
Average Support Duration	86 days

**Includes data from ongoing U.S. Phase II Pivotal Trial, which is not individually summarized for this submission.*
† Nine patients survived and went on to transplant and 12 patients are ongoing

Table 2 **Worldwide Patient Disposition**

Number of Patients Implanted	***N=229****
Number of Patients Transplanted	96
Number of Patients Continuing on Device	18
Number of Patients Died on Support	101
Number of Discontinued Patients	14

**Includes data from ongoing U.S. Phase II Pivotal Trial, which is not individually summarized for this submission*

10.2. U.S. Feasibility Study: IDE # G000091

10.2.1. Objectives

A Feasibility Study was conducted evaluating the safety of the DeBakey VAD® (without CBAS™ coating) in humans as a bridge to cardiac transplantation. Primary endpoints for the trial included survival to 30 days post heart transplant, improved NYHA Functional Class, absence of any significant neurologic deficit 30 days post transplant, and an average pump index of 2.0 l/min/m^2 or better while on device support.

10.2.2. Methods

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The Feasibility Trial was a single arm, open label, multi-center trial. The intent was to maintain the patient on mechanical circulatory support as viable transplant candidates until an appropriate donor heart became available. Following implantation, all patients were monitored until transplantation or death. To be considered a success, patients must have survived to 30 days post transplant with acceptable neurologic function, be NYHA Functional Class III or better, and have maintained an average pump index of 2.0 l/min/m^2 while on support.

10.2.3. Description of Patients

A total of 30 patients were enrolled in the Feasibility Study at three sites. All patients were accepted by the institutions' cardiac transplant committee and were NYHA Functional Class IV heart failure. All patients met all the listed inclusion/exclusion criteria: similar to that employed in other clinical trials for ventricular assist devices now commercially approved. Criteria were designed to avoid gender bias in patient enrollment.

The following tables detail Patient Baseline Characteristics for the U.S. Feasibility Trial.

Table 3 **U.S. Feasibility Study - Baseline Characteristics**

Within 48 hours prior to implant	***N=30***	***Range***
Age (years)	53	20-69
Number of Males	20	
Body Surface Area (m^2)	1.92	1.3 - 2.34

10.2.4. Results

Of the 30 DeBakey VAD® implantations performed, 20 patients survived to post transplant; survival rate was 67%. Nineteen of 20 patients met success criteria and survived to 30 days post transplant, were neurologically intact and had a NYHA III or better with a pump index during support $\geq$2.0 l/min/m^2; success rate was 63%. The remaining patient (1 of out 20) expired prior to 30 days post transplant.

The following tables detail Patient Disposition and Causes of Death for the U.S. Feasibility Trial.

Table 4 **U.S. Feasibility Study – Patient Disposition**

Status	***N=30***
Number of Patients Implanted	30
Number of Patients Completing the Study	30
Number of Patients Transplanted	20
Number of Patients Died on Support	9
Number of Patients Discontinued the Study	1
Cumulative Support Duration	1,260 days (3.5 years)
Average Support Duration	42 days
Support Duration Range	9-111 days

Table 5 **U.S. Feasibility Study Causes of Death On Support**

Cause of Death	***Device Related***	***Support Duration N=9***
Multi-organ Failure (3)	No	111
	No	79
	No	19
CVA (2)	No	90
	No	76

Bleeding (1)	Yes	73
Pulmonary Embolism (1)	No	46
Status Epilepticus (1)	No	38
Right Heart Failure (1)	No	16

Ten study subjects expired pre-transplant. Nine patients died while on support; the remaining patient died off support but with the pump *in situ*. The outflow graft was ligated due to risk of ventricular thrombi, and the pump left in place. The patient was discontinued from study participation and died shortly thereafter. This death is not reported in the table; the death did not occur while the patient was on support. Of the 10 deaths, only one was judged by the investigator to be device-related.

10.2.5. Pump Performance

10.2.5.1. Device Blood Flow

The following figure, Figure 1 illustrates the trend in pump flow within the average support duration of 42 days. Data was plotted to only 60 days, after which the sample size was too small for analysis.

Flow is consistently maintained between 4-6 l/min. With an average BSA of 1.92m^2, these flows afford pump indices between 2-3 l/min/m^2: a clinically acceptable range for end stage heart failure patients.

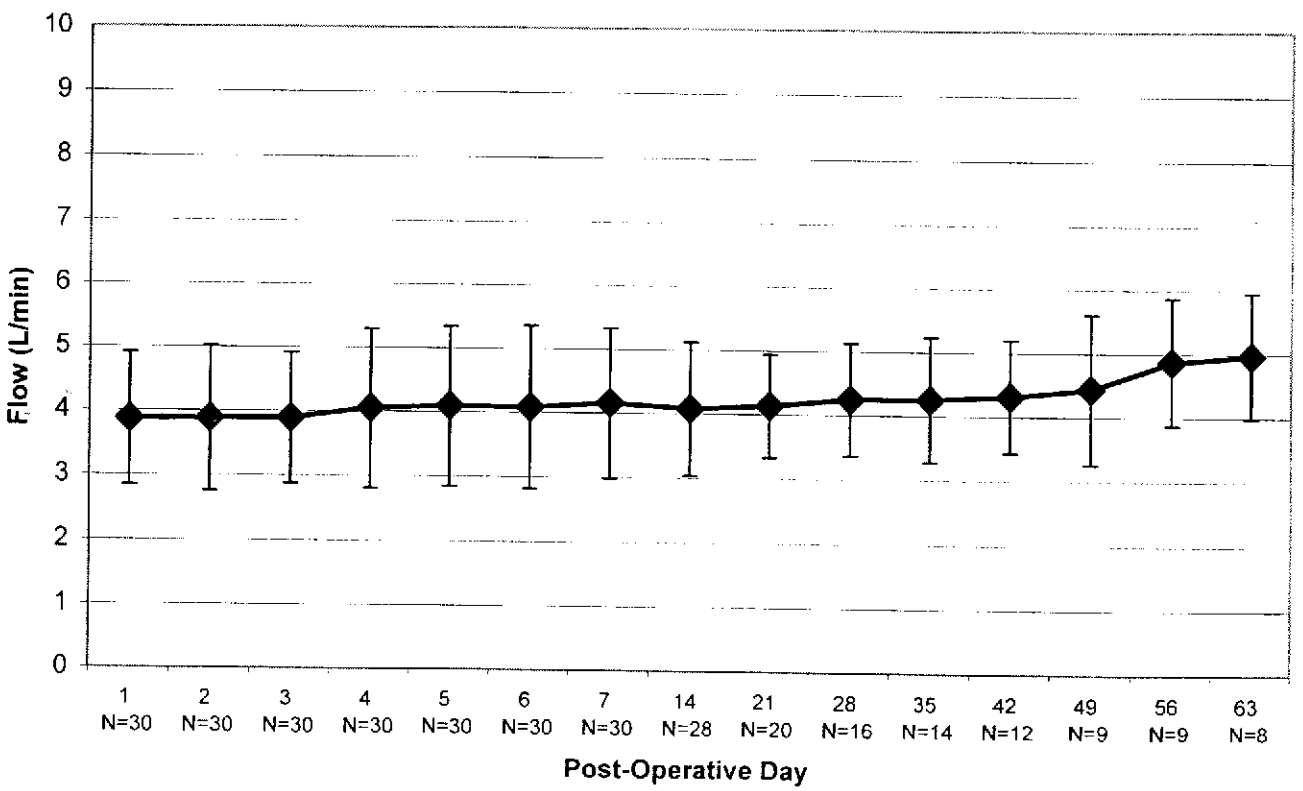

Figure 1 - Average Pump Flow: U.S. Feasibility Trial

10.2.5.2. End Organ Function

The following figure, Figure 10.2.5.2, illustrates end organ function, measured by creatinine, bilirubin and BUN, during 60 days of support, with a trend towards improvement.

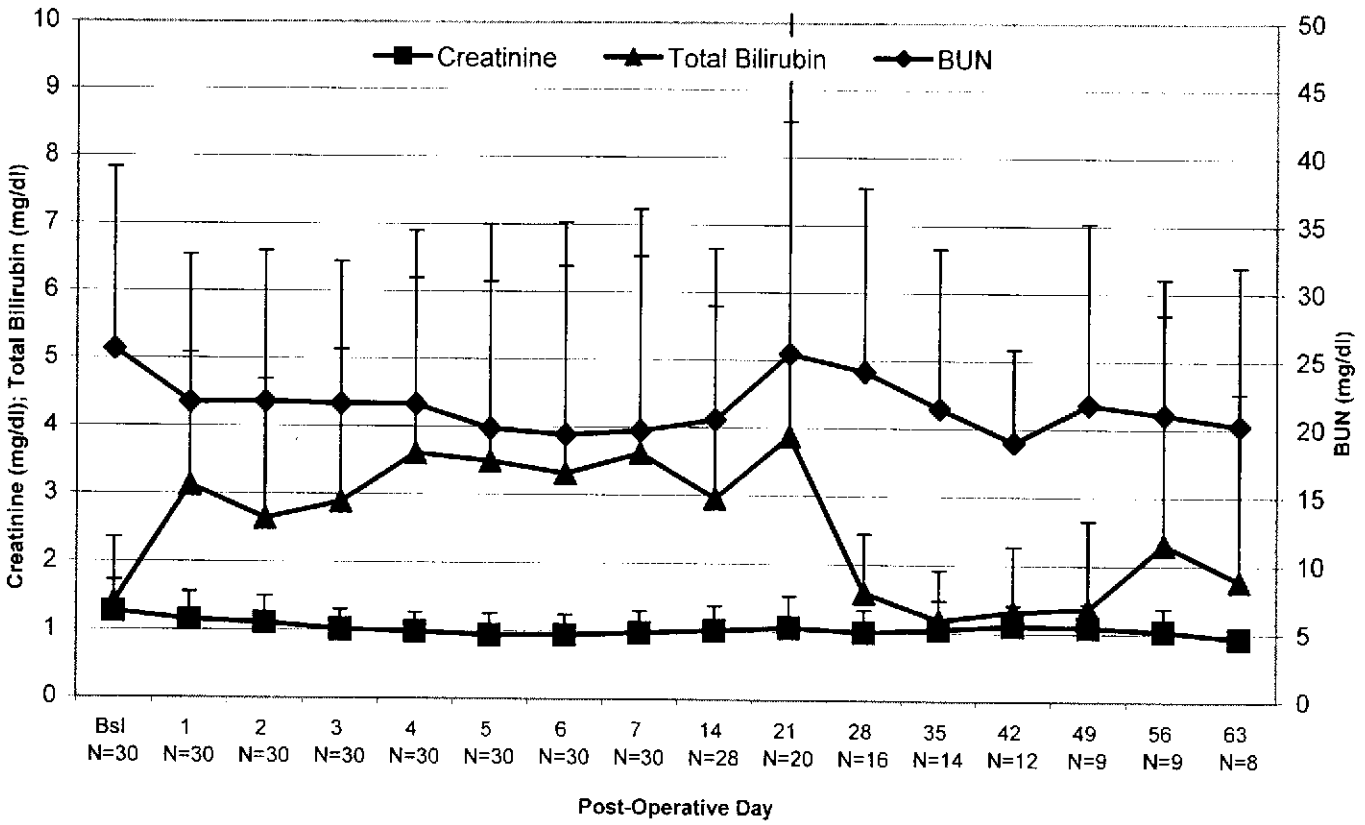

Figure 2 - End Organ Function: U.S. Feasibility Trial

The normal range for each laboratory parameter shown follows. When interpreting data, it should be understood that the normal ranges listed are for healthy adults, not patients with chronic heart failure.

BUN	8-24 mg/dl
Creatinine	0.5-1.5 mg/dl
Total Bilirubin	0.2-1.2 mg/dl

10.2.6. Observed Clinical Trial Adverse Events

The following table identifies a summary of adverse events reported during the U.S. Feasibility Trial for the DeBakey VAD® System.

Table 6

Summary of Adverse Events Reported
DeBakey VAD® U.S. Feasibility Trial
Bridge to Cardiac Transplantation in Adults

Adverse Event Type	Number of Patients With Event N=30	Percent Patients Experiencing at Least One Episode of Event
Infection	21	70%
Bleeding	16	53%
Respiratory Failure	13	43%
Cardiovascular	9	30%
Hepatic Dysfunction	8	27%
Renal Failure	6	20%
Neurologic* (CVA/TIA)	4	13%
Pump Thrombus	4	13%
Hemolysis	3	10%
Right Ventricular Failure	3	10%
Infection: device related	2	7%
Neurologic Other	1	3%
Peripheral Thromboembolism	1	3%
Mechanical Failure	0	0
Other**	9	30%

** Neuro CVA/TIA includes 3 CVAs of which 2 were minor and 1 TIA*
*** "Other" includes all single adverse events that did not meet the definition for another event type.*

Note: The most frequently occurring adverse event was infection, followed by bleeding and other components of multiorgan failure. Only two infections reported were device related; all others were hospital-acquired infections.

10.3. European Experience

Two trials were conducted in Europe; both evaluated the safety and effectiveness of the DeBakey VAD® in humans as a bridge to cardiac transplantation. The first trial used the original DeBakey VAD® blood pump (N=78); this trial is completed. The second trial evaluated the Carmeda-coated DeBakey VAD® (CBAS™ Trial: N=56); the trial is closed, however data management and analysis is ongoing. Following CE approval in Europe, DeBakey VADs were implanted on a commercial basis (N=37). Where available, data for commercial patients is included.

10.3.1. Objectives

Indications for use for the DeBakey VAD® in clinical trials was as a bridge to cardiac transplant.

10.3.2. Methods

In the initial trial, 78 patients were implanted with the DeBakey VAD® with the intent of maintaining them as viable transplant candidates until an appropriate donor heart

became available. In the CBAS™ trial, 56 patients were implanted with the Carmeda-coated DeBakey VAD®.

10.3.3. Description of Patients

The profile of the European patient was comparable to that in the U.S. Feasibility Trial population. Average age was 46 years (range 12 - 69 years) while the average body surface area was 1.87m^2 (range 1.38 – 2.31). Patients implanted with the DeBakey VAD® in both the original and CBAS™ trials were accepted by the institution's cardiac transplant committee and were functionally NYHA Class IV. They had no contraindications to cardiac transplantation at the time of implantation, or concomitant problems that would unreasonably increase the risk of ventricular assist device implantation.

During the CBAS™ trial and once commercialized, several factors influenced patient selection in Europe resulting in a lower survival rate: the DeBakey VAD® had CE Mark approval and was available on a commercial basis; commercial patient selection, and as a result CBAS™ trial patient selection, broadened beyond the inclusion/exclusion criteria for the original clinical trial. The stringent FDA mandates that regulate patient selection in the U.S. were not applicable in Europe;

10.3.4. Results

Forty-three patients from the European experience have been discharged home to await cardiac transplant. The survival to transplant rate is lower in the Europe than in the U.S, mostly attributable to earlier experience with the DeBakey VAD®, variations in the practice of medicine, protocol deviations, and the fact that a small number of patients were implanted even though it was later determined that they were not candidates for cardiac transplantation. In the original trial, 38 of 78 patients implanted survived to transplant (49%), whereas is the CBAS™ trial, 16 of 54 survived to transplant (30%); 6 of 17 commercial patients survived to transplant (35%).

The following 2 tables detail patient disposition and causes of death for the European experience. Not all data is available at this time.

Table 7 European Experience - Patient Disposition (as of Dec. 31, 2004)

Status	***Original Study N=78***	***CBAS™ Study* N=56***	***Commercial† N=37***
Number of Patients Continuing Support	0	1	7
Number of Patients Completing Study	78	55	30
Number of Patients Transplanted	38	16	11
Number of Patients Died on Support	33	37	18
Number of Patients Discontinued	7	2	1
Protocol Deviations	2	1	
Device Exchanges	4	1	
Pump Stops, Outflow ligated	1		1
Cumulative support duration	7,585 days (20.7 yrs)	6,775 day (18.6 yrs)	2,459 days (6.7 yrs)
Average support duration	75.3 days	121 days	66.5 days
Support range	0-439 days	2-518 days	0-229 days
Longest support duration		518 days	229 days
Patients supported > 6 months		14	1
Patients supported >1 year		4	0

**Data management and analysis is ongoing for the CBAS™ trial.*
†Only patient outcome is reported for the commercial patient cohort.

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In the original European trial, 7 patients were discontinued from the original study; two resulted from protocol deviations where the devices were explanted, both at the discretion of the physician. One patient was presumed to have recovered; the second patient was discontinued from anti-coagulation therapy and the device was removed. Device exchange took place in 4 patients: 2 due to pump thrombus and in 1 patient due to a connector defect. The 4th device was explanted due to Bi-VAD insertion for severe bi-ventricular failure. Ligation occurred in 1 patient due to a pump stop resulting from a wire break.

During the CBAS™ trial, 2 patients were discontinued. One patient had a device exchange due to suspected pump thrombus; the other had the device explanted for recovery and did well.

One commercial patient had the pump ligated due to pump thrombus.

Table 8 Causes of Death

Cause of Death	***N = 33***
Multi-organ Failure	21
Intracerebral hemorrhage due to anticoagulation therapy	6
Right Heart Failure	2
Encephalopathy	1
Sepsis	1
Pulmonary Failure	1
Unexplained Cable Disconnect*	1

**Circumstances suggest that this may represent a patient attempt at suicide.*

Thirty-three patients out of 78 from the original European trial died while on support. Five deaths were judged to have a possible relationship to the device. In the CBAS™ trial, the principal cause of death was consistent with the original trial: multi-organ failure and bleeding

10.3.5. Pump Performance

10.3.5.1. Original European Trial

The following figures illustrate pump performance for the original European trial. Figure 3 illustrates the trend in pump performance for 90 days of support. Flow is nearly 5 l/min for the entire time period. This flow would be sufficient to provide a 2.5 l/min/m^2 cardiac index: a clinically adequate perfusion in patients with heart failure. Figure 4 illustrates end organ function, measured by creatinine, bilirubin and BUN across 90 days of support.

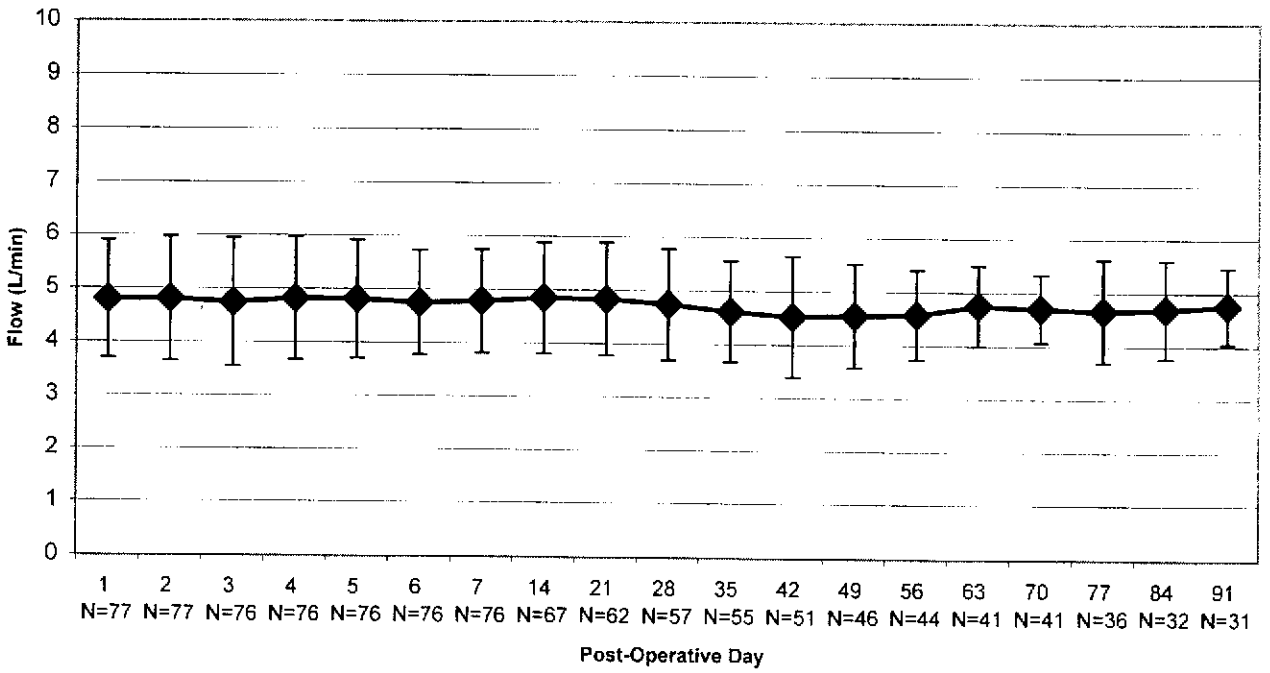

Figure 3 - Pump Flow: Original European Trial

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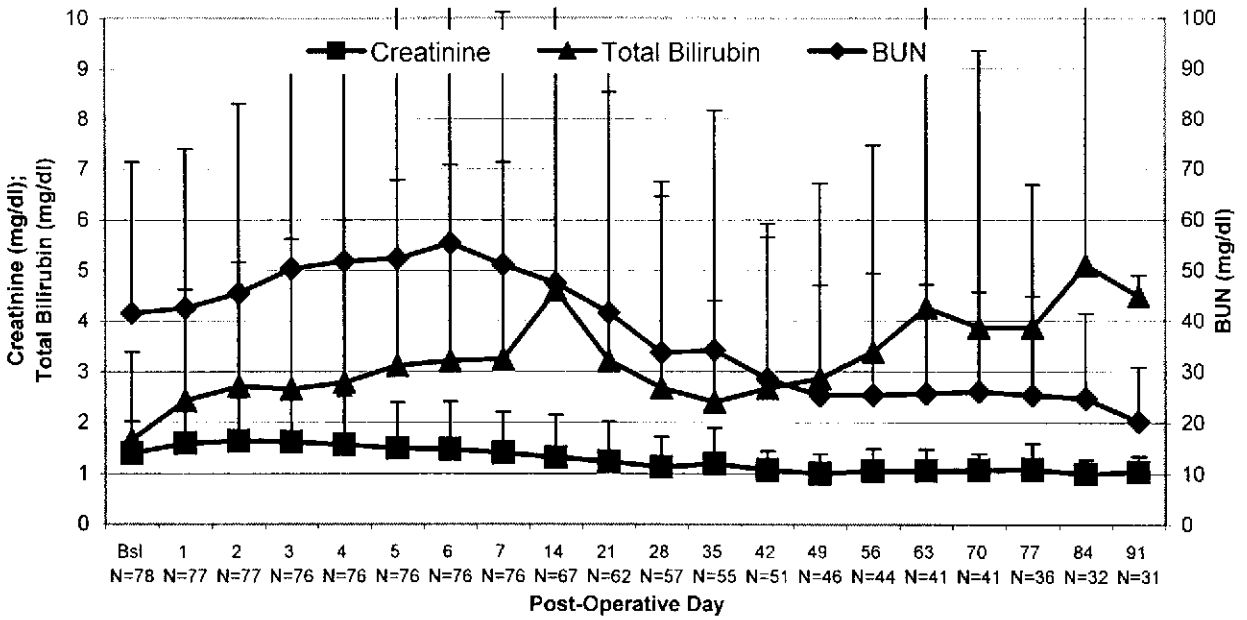

Figure 4 – End Organ Function: Original European Trial

The normal range for each laboratory parameter shown follows. When interpreting data, it should be understood that the normal ranges listed are for healthy adults, not patients with chronic heart failure.

BUN	8-24 mg/dl
Creatinine	0.5-1.5 mg/dl
Total Bilirubin	0.2-1.2 mg/dl

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10.3.5.2. CBAS™ Experience

The following figure, Figure 5 illustrates the trend in pump flow for 60 days of support using a CBAS™ coated pump. Pump flows were maintained at approximately 4 l/min across the time period.

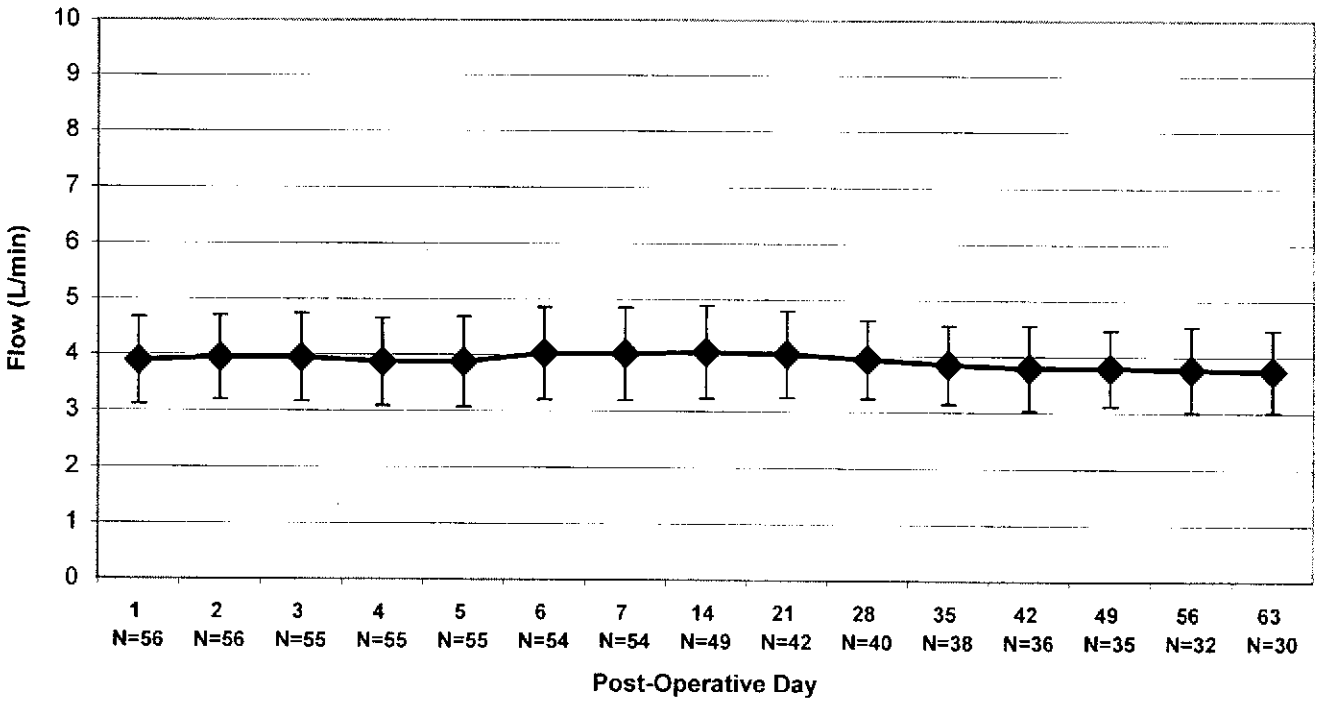

Figure 5 – Pump Flow: CBAS™

Figure 6 illustrates the trend in end organ function, measured by creatinine, bilirubin and BUN. Data suggests an improvement in end organ function overtime from elevated baseline levels. Data depicted in the figure is preliminary; outlier values are still being calculated.

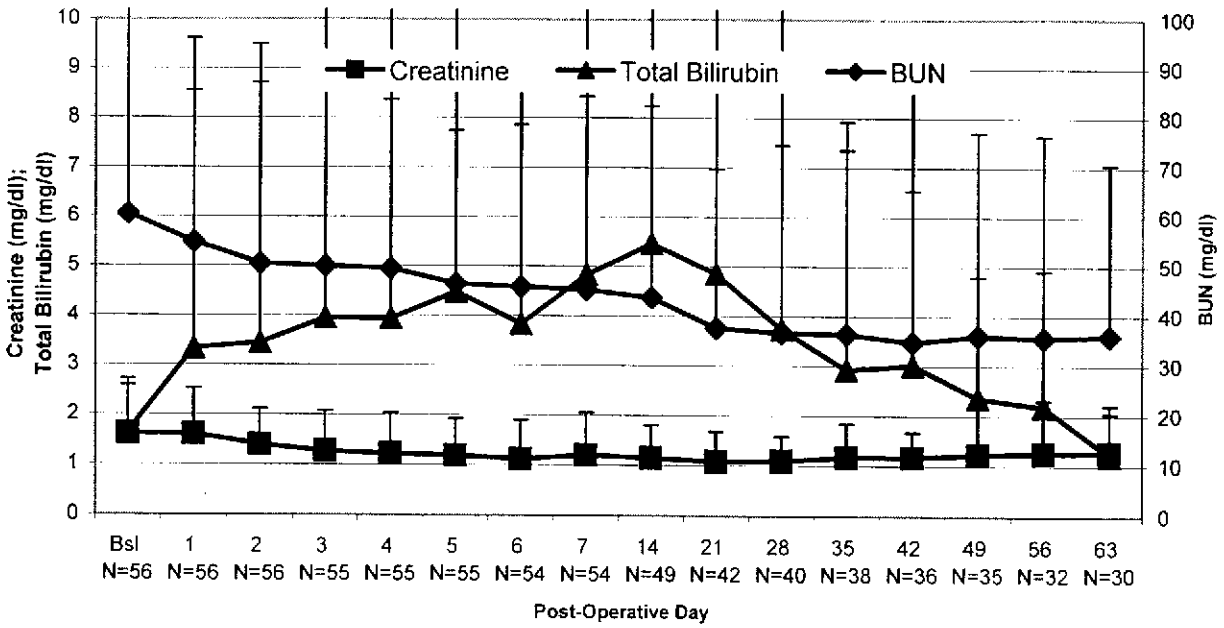

Figure 6 – End Organ Function: CBAS™

The normal range for each laboratory parameter shown follows. When interpreting data, it should be understood that the normal ranges listed are for healthy adults, not patients with chronic heart failure.

BUN	8-24 mg/dl
Creatinine	0.5-1.5 mg/dl
Total Bilirubin	0.2-1.2 mg/dl

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10.3.6. Observed Adverse Events

The following two tables report the summary of adverse events for the European bridge to transplant study for the DeBakey VAD® and the CBAS™ trial.

Table 9

Summary of Adverse Events Reported
DeBakey VAD® European Trial
Bridge to Cardiac Transplantation in Adults

Adverse Event Type	Number of Patients With Event N=78	Percent Patients Experiencing at Least One Episode of Event
Bleeding	39	50%
Infection	20	26%
Cardiovascular	17	22%
Respiratory Failure	16	21%
Hemolysis	15	19%
Renal Failure	15	19%
Neurologic Other	12	15%
Pump Thrombus	12	15%
Hepatic Dysfunction	9	12%
Neurologic (CVA/TIA)	8	10%
Right Ventricular Failure	6	8%
Mechanical Failure	4	5%
Device Related Infection	3	4%
Peripheral Thrombo-embolism	3	4%
Other	26	33%

Note: The most frequently occurring adverse events were infection and bleeding, followed by other components of multi-organ failure. Bleeding was largely attributed to instances of excess anticoagulation early in the trial. Only three infections reported were device related. Only 1 patient with a reported pump thrombus also had a thrombo-embolic stroke following pump thrombus.

Table 10

Summary of Adverse Events Reported
DeBakey VAD® CBAS™ Clinical Trial
Bridge to Cardiac Transplantation in Adults

Adverse Event Type	Number of Patients With Event N=58	Percent Patients Experiencing at Least One Episode of Event
Bleeding	37	66%
Infection	15	27%
Multi-organ Failure	12	21%
Pump Thrombus	9	16%
Hepatic Dysfunction	10	18%
Renal Failure	9	16%
Neurologic (CVA/TIA)	9	16%
Cardiovascular	7	13%
Respiratory Failure	5	9%
Right Ventricular Failure	4	7%
Hemolysis	3	5%
Device Related Infection	1	2%
Neurologic Other	0	0%
Mechanical Failure	0	0%
Peripheral Thrombo-embolism	0	0%

Note: Adverse events for the CBAS™ trial are still being adjudicated. The most frequently occurring adverse events were infection and bleeding, followed by other components of multi-organ failure.

10.4. Pump Thrombus

10.4.1. Overview

All events of pump thrombus were reported, even if they could not be confirmed in order to address potential effects of pump thrombus on patient safety. Pump thrombus was demonstrated to affect 13-16% of patients.

In the original European trial, investigators reported 12 pump thrombus events. Three of 12 events occurred before implementation of increased motor torque in the pump; increased motor torque enables the pump to better handle thrombus that might occur. One of 12 events was described as syncope due to pump stop; 2 events diagnosed as pump thrombus described only flow decreases as evidence of pump thrombus.

In the CBAS™ trial, investigators cited 9 patients experiencing 10 pump thrombus events. Pump thrombus was broadly defined, including suspected episodes where the total flow remained between 2 - 3 l/min. CBAS™ events are still being adjudicated.

Sixty-six implanted pumps had CBAS™ coating on only the inside surface, with a pump thrombus rate of 15%.

Explant analyses confirmed thrombus in the rear hub area of the device in 8 of 25 patients reported to have pump thrombus. Explant analyses could not confirm pump thrombus in all cases; thrombolytic therapy was frequently used to treat the suspected

pump thrombus possibly resulting in dissipation of the suspected clot, or provided the opportunity for evidence of pump thrombus to either be reduced or augmented by subsequent exposure to blood flow. As such, the number of pump thrombus events reported reflects a conservative tally; pump thrombus events may be overestimated.

Note: 11 of 25 patients (44%) with a reported pump thrombus went on to successful transplant. Only 1 pump thrombus resulted in permanent impairment from thrombo-emboli.

10.4.2. Pump Thrombus Mitigation

To reduce the incidence of pump thrombus, motor torque was increased in the pump, enabling the impeller to rotate more freely. Following identification of a link between high current draw and pump thrombus, discharge protocol criteria instructs patients to return to the hospital if an excess current alarm cannot be silenced, or if multiple excess current alarms occur a 24 hour period. CBAS™ coating is now applied to both internal blood contacting components of the pump and the outer surface of the inflow cannula that extends into the left ventricle.

10.5. Device Malfunctions: Worldwide

10.5.1. U.S Device Malfunctions

There were no mechanical failures reported during the U.S. Feasibility trial and during the CBAS™ trial.

10.5.2. European Device Malfunctions

During the original European trial, three patients experienced pump stops. Two pump stops were the result of a connector defect; the third pump stop was caused by a wire separation. Following corrective actions, no similar system failures occurred. Full details of the device malfunctions are contained in the clinical experience reported in Volume I, Section 8 of this submission, *Clinical Experience*.

10.6. Conclusions to be Drawn from the DeBakey VAD® Clinical Studies for the DeBakey VAD® Child

The DeBakey VAD® *Child* is virtually the same device as the DeBakey VAD® System used in adults, save for minor modifications to accommodate a better fit in children. The DeBakey VAD® *Child* is expected to be functionally and hemodynamically similar to the adult version of the DeBakey VAD®, with a performance envelope that encompasses the appropriate flows for the physiologic needs of children in the intended age group: 5 years to 16 years old.

Analysis and review of a BSA Nomogram indicates that a patient with a $0.7m^2$ BSA is equivalent to 38 lbs. An individual weighing 38 lbs in the 50^{th} percentile is approximately five years of age. A 5 year old normally has a mean cardiac index of 3.7 l/min/m^2. Adjusting the cardiac index to a BSA of $0.7m^2$ yields a desired pump flow of 2.6 l/min (3.7 x 0.7 = 2.59 rounded to 2.6 l/min). The performance envelope for the DeBakey VAD® *Child* demonstrates that the DeBakey VAD® *Child* has the capacity to deliver flow of 2.6 l/min between 7500 and 8500 RPM, thereby supporting the minimum cardiac output required for a 5 year old patient with a BSA as low as $0.7m^2$.

11. DeBakey VAD *Child* Probable Benefits

The DeBakey VAD® *Child* is expected to provide the same benefits for children that the adult version has provided for adults: i.e. total left ventricular unloading and support in end stage heart failure with a low incidence of device related infections and opportunity for survival rate consistent

with the Feasibility Trial. Pump performance data for the adult DeBakey VAD® in conjunction with the performance envelop for the DeBakey VAD® *Child* suggest flow rates that will meet the level of output required to support pediatric patients.

The probable benefits associated with the DeBakey VAD® *Child* are: 1) adequate ventricular circulatory support; 2) improved qualify of life from an implantable and more appropriate device size; 3) ease of implantation and reduced surgical time; 4) uncomplicated post-operative recovery with reduced infection rate; 5) and early mobilization and greater mobility for the child.

Risks associated with the DeBakey VAD® are consistent with those associated with commercially approved devices and alternative treatment options. Currently available mechanical circulatory support options for pediatric patients with end stage heart failure are limited by low survival rates and complications, such as infection, bleeding and neurologic events. ECMO is limited to those patients who require respiratory support in addition to cardiac support. Patients with ECMO and centrifugal pumps are immobilized. Thoratec patients have limited mobility; device design such as blood volume priming requirements, lack of portability, and device size and external placement on the abdomen inhibits use of this device in all but the very large pediatric patient.

Although survival to transplant rates in the European experience have ranged from 30-49%, the low incidence of device related infection and the survival to transplant rate of 67% reported in the Feasibility Trial associated with the adult DeBakey VAD outweigh the risks of the DeBakey VAD *Child*. This risk-benefit ratio is highlighted when taking into account the risks and benefits associated from alternative methods of treatment, and from the morbidity and mortality associated with Class IV heart failure in children between 5 years and 16 years old.

12. Panel Recommendation

A Circulatory System Devices Panel Advisory Meeting was not held to discuss this device. However a general Panel meeting was held where a lengthy discussion of clinical requirements for this category of devices in children requiring temporary mechanical circulatory support took place. Based on a review of these recommendations and the data in the HDE, it was determined that a full Panel meeting was not necessary for this HDE.

13. CDRH Decision

CDRH determined that, based on the data submitted in the HDE, the DeBakey VAD *Child* will not expose patients to an unreasonable risk of illness or injury, and the probable health benefit from using the device outweighs the risk of illness or injury.

CDRH issued approval on FEB 25 2004.

14. Approval Specifications

14.1. Indications for Use

See the *Directions For Use*

14.2. Hazards to Health from use of the Device

See Contraindications, Warnings and Precautions, and Adverse Events in the *Directions for Use*

14.3. Post approval Requirements and Restrictions

See Approval Order

Changes
(Items in red reflect rationale for not making changes)

1. Section 1: Changed HUD designation to HDE designation

2. Section 2: Inserted the word *Child* into the indications for use, first line: from DeBakey VAD to DeBakey VAD *Child*

3. Section 3: Added body surface area to contraindications

4. Sections 6, 7, and 8 were renumbered to be consistent w/ template

5. Section 8: Information previously contained under Observed Adverse Event was moved to Section 10: Summary of Clinical Studies

6. Section 9: PreClinical Summary was reformatted to address Bench Testing and Animal Studies per template. The Reliability Testing Section 9.1.3 was revised to add more information.

7. Sections 10.1 and 10.3: Data was updated to be current as of December 31, 2004

    a. Figures 1-6 in Section 10 were modified as follows:
        i. Duplicate graph title was cleared
        ii. Y-axis labels and number fonts were increased to 11-14
        iii. X-axis labels and number fonts were increased to 9-14
        iv. For each data series
        v. The symbol was increased to size 10
        vi. The weight of the line was increased
        vii. The color of the data series was modified to be black
    b. Standard deviations were added to each data series. On end organ function graphs SD bars were placed in only one direction to improve clarity of the graph

    Note: Because three laboratory values are plotted in one end organ graph, lines for normal ranges were not applied since six additional lines would make the graph impossible to read. Additionally, normal ranges for the laboratory measures performed would not reflect the normal range for chronic heart failure patients.

    c. A paragraph was added listing the normal ranges for BUN, creatinine, and bilirubin for healthy adults below each end organ function graph.

8. Section 10.2.6 and 10.3.6: Information formerly included under Adverse Events (old Section 6.2.1 US Experience) was moved to follow Section 10.2.5.2 and 10.3.5. Information was split to conform to the split in reporting US and European data; US Adverse Events follows as Section 10.2.6 and European Adverse Events follows as Section 10.3.6.

Note: The recommendation was made to put AE reporting to follow 10.2.5.2. However, this recommendation would have put European AEs in the U.S. section.

9. Section 10: As a result of reformatting Clinical Data to make the document consistent with the Template, all tables have been renumbered.
    a. Table 1 is now Table 6
    b. Table 2 is now Table 9
    c. Table 3 is now Table 10
    d. Table 4 is now Table 1
    e. Table 5 is now Table 2
    f. Table 6 is now Table 3

g. Table 7 is now Table 4
h. Table 8 is now Table 5
i. Table 9 is now Table 7
j. Table 10 is now Table 8

10. Sections 10.2.6. and 10.3.6.: Header (Bridge to Cardiac Transplantation in Adults) was inserted into Tables 9, and 10 consistent with the change made by FDA in Table 6 (Summary of AEs for European Trial, Summary of AEs for CBAS trial and Summary of AEs for US Feasibility Trial, respectively).

Note: This change was not inserted into Table 1 as suggested (Worldwide Patient Distribution), since this represented a different type of table compared to Tables 6, 9, and 10, and since the change was not suggested for Tables 2, 3, 4, and 5 which are similar to Table 1.

11. Section 10. 5., now includes Device Malfunctions. Information was split to be consistent with data reporting for US and European. US malfunctions are now reported under section 10.5.1 and European device malfunctions are reported under section 10.5.2.

Note: The recommendation would have put Device Malfunctions immediately following AEs, which would have grouped worldwide malfunctions under US data.

12. Former Section 10.5: All information related to Device Complaints has been deleted since it represents duplication information.

13. Section 10.6 now includes Conclusions to be Drawn

14. Former Section 11.1 has been deleted since it represents duplicative information

15. Former Section 11.3 was reformatted and included in Section 11 (Probable Benefits)

16. Section 12: Added template statement on not going to Panel.

17. Section 14: Post Approval Requirements and Restrictions subsection (14.3) was added

18. Section 15 was omitted since no references were used for this section.

19. Section 11.0 was modified to reflect the European rates for survival to transplant.